

CLAIMS

We claim:

1. A conjugate comprising a first sequence and a second sequence, wherein the first sequence comprises a transport protein or a polynucleotide encoding a transport protein and the second sequence comprises a polypeptide or polynucleotide that modulates Notch signalling.
2. The conjugate according to claim 1, wherein the conjugate is a fusion protein.
3. The conjugate according to claim 1, wherein the second sequence is a polypeptide or polynucleotide for Notch signalling transduction.
4. The conjugate according to claim 3, wherein the second sequence is Notch, or a fragment thereof which retains the signalling transduction ability of Notch, or an analogue of Notch which has the signalling transduction ability of Notch, or a polynucleotide sequence which encodes therefor.
5. The conjugate according to claim 4, wherein the second sequence is Notch intracellular domain (Notch IC), or a polynucleotide sequence that encodes therefor.
6. The conjugate according to claim 4, wherein the second sequence is an Epstein Barr virus (EBV) protein, or a polynucleotide sequence that encodes therefor.
7. The conjugate according to claim 6, wherein the second sequence is EBNA2, BARF0 or LMP2A, or a polynucleotide sequence that encodes therefor.
8. The conjugate according to claim 1, wherein the second sequence is a polypeptide or polynucleotide that activates Notch signalling.
9. The conjugate according to claim 8, wherein the second sequence is a dominant negative version of a Notch signalling repressor, or a polynucleotide encoding a dominant negative version of a Notch signalling repressor.
10. The conjugate according to claim 8, wherein the second sequence is a polypeptide or polynucleotide which inhibits the expression or activity of a Notch signalling repressor, or a polynucleotide encoding said polypeptide.
11. The conjugate according to claim 1, wherein the second sequence is an agent that acts in the nucleus or a polynucleotide encoding said agent.

12. The conjugate according to claim 1, wherein the second sequence is a Notch signalling transcription factor or a polynucleotide encoding a Notch signalling transcription factor.

13. The conjugate according to claim 1, wherein the second sequence is a DNA binding agent or a polynucleotide encoding a DNA binding agent.

14. The conjugate according to claim 1, wherein the second sequence is a polypeptide comprising a Notch Ankrin domain or a polynucleotide encoding a polypeptide comprising a Notch Ankyrin domain.

15. The conjugate according to claim 14, wherein the second sequence further comprises a RAM domain, a PEST sequence, an OPA sequence or a polynucleotide encoding a RAM domain, a PEST sequence or an OPA sequence.

16. The conjugate according to claim 1, wherein the second sequence is a polypeptide or polynucleotide that inhibits Notch signalling.

17. The conjugate according to claim 16, wherein the second sequence is a dominant negative version of a Notch signalling activator or transducer, or a polynucleotide encoding a dominant negative version of a Notch signalling activator or transducer.

18. The conjugate according to claim 16, wherein the second sequence is a polypeptide or polynucleotide that inhibits the expression or activity of a Notch signalling activator or transducer, or a polynucleotide encoding a polypeptide that inhibits the expression or activity of a Notch signalling activator or transducer.

19. The conjugate according to claim 16, wherein the second sequence is a polypeptide capable of downregulating the expression or activity of Notch, a Notch ligand or a downstream component of the Notch signalling pathway, or a polynucleotide that encodes therefor.

20. The conjugate according to claim 19, wherein the second sequence is selected from the group consisting of Toll-like receptors, bone morphogenic proteins (BMPs), BMP receptors, activins, derivatives, fragments, variants and homologues thereof, and a polynucleotide that encodes therefor.

21. The conjugate according to claim 1, wherein the first sequence is a nuclear localisation protein.

22. The conjugate according to claim 1, wherein the first sequence is a herpesvirus VP22 protein (VP22) or a fragment thereof that retains a VP22 transport function.

23. The conjugate according to claim 22, wherein the first sequence is a full length VP22 sequence.

24. The conjugate according to claim 22, wherein the fragment of VP22 comprises:

from about amino acid 60 to about amino acid 301 of the full length VP22 sequence,

or

from about amino acid 159 to about amino acid 301 of the full length VP22 sequence.

25. The conjugate according to claim 1, wherein the first sequence comprises a homeodomain, or a variant thereof that retains a transport function.

26. The conjugate according to claim 25, wherein the homeodomain is from Antennapedia, Fushi-tarazu or Engrailed.

27. The conjugate according to claim 1, wherein the first sequence is an HIV tat protein, or a variant thereof that retains a transport function.

28. A polynucleotide sequence encoding the conjugate of claim 1.

29. An expression vector comprising the polynucleotide sequence of claim 28.

30. A host cell transformed with the expression vector of claim 29.

31. A method for preparing a conjugate comprising culturing the host cell of claim 30 under conditions which provide for the expression of the conjugate.

32. A conjugate prepared by the method of claim 31.

33. A method of transforming a cell with a protein for Notch signalling modulation or a polynucleotide sequence which encodes therefor, the method comprising introducing the expression vector of claim 29 into the cell.

34. A composition comprising the conjugate of claim 1 and a pharmaceutically acceptable excipient, diluent or carrier.

35. A method for the prevention or treatment of disease or infection comprising administering the composition of claim 34 to a subject in need thereof.

36. The method according to claim 35, wherein the disease is a T-cell mediated disease.